throughout the specification as filed, such as at the paragraph bridging pages 6 and 7 of the instant specification. No new matter has been added.

Applicants take this opportunity to address the rejection advanced by the Examiner in the Final Office Action dated June 17, 1999. For reasons detailed below the rejection is overcome by the remarks below.

Remarks

Claims 57-61, 71, 74, and 77-78 and 79-89 will be pending upon entry of this amendment. Reconsideration of the one rejection made in the Official action is respectfully requested.

(i) **Rejections under 35 U.S.C. § 112, first paragraph**

The Examiner has rejected claims 57-61, 71, 74 and 77-78 under 35 U.S.C. § 112, first paragraph, for lack of enablement. More particularly, the Examiner alleges:

> *No biological activities have been specifically demonstrated for EMAP III. The assertion that EMAP III has similar biological activities as EMAP II cannot be accepted in the absence of supporting evidence, because the relevant literature reports examples of closely related polypeptides belonging to a polypeptide family wherein individual members have distinct, and sometimes even opposite, biological activities . . . Thus, the specification fails to teach the skilled artisan how to use EMAP III and variants thereof without resorting to undue experimentation to determine what the specific biological activities of EMAP III are.*
>
> *The specification does not teach the skilled artisan how to use the disclosed EMAP III for purposes unrelated to the asserted biological activity. For example, there is no evidence of tissue-specific expression patterns, such that the EMAP III protein could be used as a tissue-specific marker. Similarly, there is no disclosure of particular disease states correlating to an alteration in levels or forms of EMAP III such that EMAP III could be used as a diagnostic tool, Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polypeptides or [sic] any purpose.*
>
> *Due to the large quantity of experimentation necessary to determine an activity or property of EMAP III such that it can be determined how to use EMAP III, the lack of direction/guidance presented in the specification regarding same, the absence of working examples direct to same, the complex nature of the invention, and the state of the prior art establishing that biological activity cannot be predicted based on structural*

similarity, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicants respectfully traverse this "how to use" rejection for the following reasons. The specification need not describe all the uses to which the claimed invention may be put and need not disclose matter that is known to persons of skill in the art. The specific purpose for which the claimed invention may be used must be either (1) described in the instant specification or (2) evidence may be introduced showing that the reported properties of the claimed invention are sufficient to justify the conclusion that the claimed invention is useful for a specific purpose.

The instant specification does describe purposes for which the claimed invention may be used. First, the specification points out that the EMAP III polypeptide of the claimed invention may be employed to regress neoplasia, such as tumors, in cancers. See page 15, third full paragraph. Methods for using a polypeptide in neoplasia regression are well known to the skilled artisan and, therefore, need not be disclosed. Neoplasia regression includes, for example, anti-proliferative effects on cancer cells and tissues, as well as antiangiogenic effects *in vitro or in vivo*. Methods for showing these anti-proliferative and antiangiogenic effects are well known to one of skill in the pertinent art. See, for example, methods for assaying tumor vascular development referenced and employed in Schwarz et al., Am. J. Physiol 276: L365-75.

Second, the claimed invention may be used in a diagnostic assay for detecting altered levels of the polypeptide of the present invention in various tissues. See page 22 at lines 4 through 8. Methods for detecting the altered levels of a polypeptides in various tissues are not only described in the instant specification at page 22 line 9- page 23 line 9, but are well known to the skilled artisan.

Third, the claimed polypeptides and fragments, or cells expressing such, can be used as an immunogen to produce antibodies specific for EMAP III. See page 24, bottom paragraph. Methods for using a protein as an immunogen are not only described in the instant specification at page 25, lines 7- 31, but are well know to one of skill in the art.

Furthermore, no undue experimentation is required to enable the skilled artisan to use the claimed invention in a manner that are similar to EMAP II, namely (1) to activate endothelial cells and mononuclear cells to potentiate their participation in procoagulant reactions through induction of tissue factor and (2) to promote migration of monocytes and polymorphonuclear leukocytes. See specification at page 2, lines 6-15. The skilled artisan could readily determine

how to use EMAP III for these purposes because methods for doing so are well known to persons of skill in the art, as described, for example, in Kao et al., J. Biol. Chem 267(28): 20239-47 (1992).

In summary, one of ordinary skill in the art would recognize that the above-recited uses for EMAP III, which are identified in the instant specification, enable one of skill in the art to use the claimed invention.

V. Conclusion

Applicants respectfully request that the remarks of the present response be entered and made of record in the present application. The application is believed to be in condition for allowance. Early notice to that effect is earnestly solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below. If a fee is required in connection with this paper, please charge Deposit Account No. 08-3425 for the appropriate amount.

Respectfully submitted

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